REMARKS

The Examiner provides a number of rejections and we list them here in the order in which they are addressed:

I. Claims 1-20 are rejected under 35 U.S.C. § 112 ¶ 1 as allegedly containing matter which was not described in the specification.

II. Claims 1-20 are rejected under 35 U.S.C § 103(a) as allegedly being unpatentable over Anderson *et al.* (US Pat. No. 5,922,591) in view of Wilding *et al.* (US Pat. No. 5,587,128) and Yamaguchi *et al.* (US Pat. No. 3,965,047).

III. The title of the specification is allegedly non-descriptive of the claimed matter.

I. Claims 1 - 20 Meet 35 U.S.C § 112 ¶ 1 Description Requirements

The Examiner rejects the claims relying on the statement that "As presently worded, the claims encompass "microdroplet transport channels" of virtually any dimension." (*Office Action pg. 2* ¶ 4) and then argues that the Applicants' recitation of preferred dimensions on page 8 of the specification is the only basis on which to establish the intended scale of the invention. The Applicants disagree and submit that the Examiner has not given the Applicants' definition of "Channels" due consideration. For example, Applicants have carefully and specifically defined "Microdroplet transport channels":

> "Microdroplet transport channels" are channels configured **(in microns)** so as to accommodate **"microdroplets"**. *Applicants' Specification, pg. 8 ln 20 - 21.* [emphasis added]

Clearly, the Examiner may not properly interpret the Applicants use of the term "Microdroplet transport channel" as an attempt to claim channels "... virtually of any dimension" because the definition clearly contemplates channels measured in microns.

Furthermore, the microscale nature of the invention as a whole is plainly stated throughout the specification, for example:

> The present invention is related to **microfabrication** and biological reactions in **microfabricated** devices, and in particular, movement and mixing of biological

samples in **microdroplets** through **microchannels**. *Applicants' Specification, pg. 11, ln 18 -20.* [emphasis added]

The Examiner is unfairly restricting the claims to the specific exemplary dimensions recited in the specification. Nonetheless, without acquiescing to the Examiner's argument but to further the prosecution, and hereby expressly reserving the right to prosecute the original (or similar) claims, Applicants have amended the claims to recite specific dimensions of width and depth.

Furthermore, the Examiner's implication that "microdroplet transport channels" lack support in the Applicants' priority documents is also without merit for the same argument as presented above.

II. Claims 1 - 20 Are Non-Obvious

The Examiner rejects the claims as obvious based on the combination of references consisting of US Pat. No. 5,922,591 To Anderson *et al.*, in view of US Pat. No. 5,587,128 To Wilding *et al.* and US Pat. No. 3,965,047 To Yamaguchi *et al.* The Applicants disagree because the Examiner has failed to make a *prima facie* case of obviousness.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the reference(s) themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488, 20 USPQ.2d 1438 (Fed. Cir. 1991); and *MPEP* § 2142; Establishing A *Prima Facie* Case Of Obviousness. The Examiner is reminded that if ONLY ONE of the above requirements is not met, then a *prima facie* case of obviousness does not exist. In the present Office Action, the Applicants clearly demonstrate that the Examiner's rejection does not meet these criterion. The Applicants rebut the establishment of a *prima facie* case of obviousness by the argument below.

A. Anderson *et al.* Does Not Teach Heating Elements Arrayed Along Microdroplet Transport Channels

The Examiner admits that the '591 patent to Anderson *et al.* "do[es] not disclose that the heating elements are arranged in an array format such that fluid transport is achieved." The Applicants agree. Moreover, Anderson *et al.* does not provide any teachings,

either explicit or implicit, to suggest or motivate one skilled in the art to array heating elements along a microdroplet channel. In fact, Anderson *et al.* discloses heating elements only in proximity to a reaction chamber:

> A number of the operations performed by the various **reaction chambers** of the device require a controllable temperature.
>
> ...
>
> These heaters may be provided as a layer on one surface of a **reaction chamber**, or may be provided as molded or machined inserts into the **reaction chambers**. *Anderson et al.* col. 31 ln 22 - 50. [emphasis added]

Second, the Examiner does not identify, and the Applicant cannot find, any teaching within Anderson *et al.* regarding any embodiment that shows a reasonable expectation of success to provide an array of heating elements along the disclosed fluid channels.

Anderson *et al.*, therefore, adds nothing to the other two cited references of Yamaguchi *et al.* and Wilding *et al.* The Applicants respectfully submit to the Examiner that Anderson *et al.* is an improperly combined 35 U.S.C. § 103(a) reference[1].

B. Wilding *et al.* Does Not Teach Heating Elements Arrayed Along Microdroplet Transport Channels

The Examiner asserts Wilding *et al.* for teaching "... a series of heating means that are arranged along a common flow path." and then proceeds to admit that "The intent of the heating elements in the disclosure is for the denaturation of nucleic acid, not for fluid transport." *Office Action pg. 5 ¶ 12.*

The Applicants have carefully inspected Wilding *et al.* and agree that the disclosed heating elements are consistently contemplated as associated only with the reaction chambers (*i.e.*, sections 22A and 22B) and never with the fluid channels/flow path (*i.e.*, 20B). Applicants urge the Examiner to reconsider that Wilding *et al.* discloses only heating elements arrayed along a reaction chamber and not along a microdroplet transport channel. For the Examiner's convenience Applicants provide several exemplary passages:

> The device may further include a system for **thermally cycling the contents of the reaction chamber** ... *Wilding et al., col 12 ln 34 -37.* [emphasis added]

and,

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[1] It should be noted that the '591 patent is a continuation-in-part of a provisional application. Applicants reserve the right to challenge the sufficiency of the provisional (which has not yet been inspected).

> ... the reaction chamber advantageously facilitates **heat transfer to the reaction chamber contents** ... from a heater positioned near the substrate ... *Wilding et al., col 12 ln 46 - 50.*[emphasis added]

and,

> As discussed above, **reaction chamber sections may be heated** by means of an electric element integrated in the substrate below the sections, which can mate with electrical elements of the appliance. Alternatively, an optical laser may be used to **heat the reaction chamber sections** through a glass cover disposed over the substrate. *Wilding et al.* col. 23 ln 48 - 53. [emphasis added]

Wilding *et al.*, therefore, adds nothing to the other two cited references of Anderson *et al.* and Yamaguchi *et al.* The Applicants respectfully submit to the Examiner that Wilding *et al.* is an improperly combined 35 U.S.C. § 103(a) reference.

C. Yamaguchi *et al.* Does Not Teach Heating Elements Arrayed Along Microdroplet Transport Channels

The Examiner asserts Yamaguchi *et al.* for teaching "... an array of heating elements so to achieve "differential heating"." *Office Action pg 4 ¶ 9.* The Applicants assert that the Examiner has brought forth a functional argument on which to base a rejection of device claims. As the Examiner is well aware, functional language in relation to a device claim is irrelevant in the determination of patentabililty. The critical issue to evaluate the heating elements of Yamaguchi *et al.* is not whether they are capable of differential heating but whether or not they are arrayed along a microdroplet transport channel. The Applicants argue that Yamaguchi *et al.* is silent regarding any element resembling a microdroplet transport channel.

First, Yamaguchi *et al.* does not teach fluid movement through a microdroplet transport channel that generated by differential heating. Instead, Yamaguchi *et al.* teaches fluid pumping devices:

> ... a compressor, blower, fan, pump, impeller or the like, will be employed in motivating the fluid through the respective heating devices. *Yamaguchi et al.,* col 5 ln 3-7.

Second, Yamaguchi *et al.* does not provide any teachings, either explicit or implicit, to suggest or motivate one skilled in the art to attempt the invention by use of any microfabrication techniques. Third, Yamaguchi *et al.* does not provide any teaching regarding any contemplation of incorporating a microdroplet transport channel. Fourth, Yamaguchi *et al.* teaches away from any concept that the disclosed heating elements would allow any

configuration with a microdroplet transport channel. Yamaguchi *et al.*, in fact, teaches the opposite:

> The heat generating members formed in accordance with the principles of the invention are useful for heating **large volumes** of a fluid ... The heat generating members are positioned within a fluid stream flow and the fluid is caused to flow through one or more heat generating members ... *Yamaguchi et al.* col 4 ln 6 - 12. [emphasis added]

Yamaguchi *et al.*, therefore, adds nothing to the other two cited references of Anderson *et al.* and Wilding *et al.* The Applicants respectfully submit to the Examiner that Yamaguchi *et al.* is an improperly combined 35 U.S.C. § 103(a) reference[2].

D. Conclusion

The Applicants conclude that the Examiner has improperly combined the cited references consisting of Anderson *et al.*, Wilding *et al.* and Yamaguchi *et al.* Specifically, the Examiner has failed to present a *prima facia* case as defined at the outset of this section. None of the cited references disclose "heating elements arrayed along a microdroplet transport channel", therefore not all of the claim limitations are disclosed when all three cited reference as viewed as a whole. Secondly, none of the cited references provide any motivation or suggestion for thier combination. Yamaguchi *et al.* does not contemplate microfluidics, and neither Anderson *et al.* nor Wilding *et al.* suggest that microdroplet transport channels should be heated. Consequently, none of the references provide a discussion of any reasonable expectation of success to create a modification that would array heating elements along a microdroplet transport channel.

The Applicants, therefore, respectfully request the Examiner withdraw the rejection.

III. The Specification Title Is Descriptive

The Examiner considers the present title "Microscale Devices And Reactions In Microscale Devices" as not descriptive to the scope of the present device claims. The Applicants disagree as the specification is a proper continuation of applications containing reaction claims. Nonetheless, without acquiescing to the Examiner's argument but to further

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[2] Applicants also believe Yamaguchi *et al.* is non-analogous art and one skilled in the art of microfluidics would not be motivated to seek out this reference.

the prosecution, and hereby expressly reserving the right to restore the original title, Applicants have amended the title to recite "Microscale Reaction Devices".

CONCLUSION

The Applicant believes that the arguments and claim amendments set forth above traverse the Examiner's rejections and, therefore, request that all grounds for rejection be withdrawn for the reasons set above. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, the Applicant encourages the Examiner to call the undersigned collect at 617.252.3353.

Dated: April 16, 2003

Peter G. Carroll
Registration No. 32,837

MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, California 94105
617-252-3353

APPENDIX I
MARKED-UP VERSION OF REWRITTEN CLAIMS
PURSUANT TO 37 CFR § 1.121 (c)(1)(ii)

1. (Three Times Amended) A device comprising:

   i) a microdroplet transport channel in a silicon substrate, said channel having a depth between 0.35 and 50μm, having a width between 50 and 1000μm, and connecting to a reaction region; and

   ii) a series of heating elements arrayed along said microdroplet transport channel, wherein said series of heating elements are configured so as to provide differential heating.

8. (Three Times Amended) A system comprising:

   i) a microdroplet;

   ii) first and second microdroplet transport channels in a silicon substrate, said channels having a depth between 0.35 and 50μm, having a width between 50 and 1000μm, and connecting to a reaction region; and

   iii) a series of heating elements arrayed along said first and second transport channels, wherein said series of heating elements are configured so as to provide differential heating of said microdroplet by said heating elements.

13. (Twice Amended) A device comprising:

   i) a first housing portion comprising silicon;

   ii) a microdroplet transport channel in said first housing portion, said transport channel having a depth between 0.35 and 50μm, having a width between 50 and 1000μm, and connecting to a reaction region;

   iii) a second housing portion bonded to and aligned with said first housing portion thus creating an assembled housing, wherein said second housing portion is selected from the group consisting of silicon, quartz or glass; and

iv) a series of heating elements in said assembled housing arrayed along said fluid transport channel, wherein said series of heating elements are configured so as to provide differential heating.